Compositions and Methods for Non-targeted Activation of Endogenous Genes

Abstract

The present invention is directed generally to activating gene expression or causing over-expression of a gene by recombination methods *in situ*. The invention also is directed generally to methods for expressing an endogenous gene in a cell at levels higher than those normally found in the cell. In one embodiment of the invention, expression of an endogenous gene is activated or increased following integration into the cell, by non-homologous or illegitimate recombination, of a regulatory sequence that activates expression of the gene. In another embodiment, the expression of the endogenous gene may be further increased by co-integration of one or more amplifiable markers, and selecting for increased copies of the one or more amplifiable markers located on the integrated vector. In another embodiment, the invention is directed to activation of endogenous genes by non-targeted integration of specialized activation vectors, which are provided by the invention, into the genome of a host cell. The invention also provides methods for the identification, activation, isolation, and/or expression of genes undiscoverable by current methods since no target sequence is necessary for integration. The invention also provides methods for isolation of nucleic acid molecules (particularly cDNA molecules) encoding a variety of proteins, including transmembrane proteins, and for isolation of cells expressing such transmembrane proteins which may be heterologous transmembrane proteins. The invention also is directed to isolated genes, gene products, nucleic acid molecules, to compositions comprising such genes, gene products and nucleic acid molecules, and to vectors and host cells comprising such genes and nucleic acid molecules, that may be used in a variety of therapeutic and diagnostic applications. Thus, by the present invention, endogenous genes, including those associated with human disease and development, may be activated and isolated without prior knowledge of the sequence, structure, function, or expression profile of the genes.